ABC of asthma

Methods of delivering drugs

John Rees

Various inhaler devices and formulations have been developed to deliver drugs efficiently, minimise side effects, and simplify use. With the range of devices available nearly all patients can take drugs by inhalation. All the available devices used appropriately can provide adequate drug to the airways. Inhalers should not be prescribed without checking that the patient can use the device satisfactorily. This should be rechecked on subsequent visits as errors can develop and interfere with treatment. Some drugs, such as leukotriene receptor antagonists and theophylline, cannot be given by inhalation.

Metered dose inhalers

Inhalers deliver the drug directly to the airways. Even when a metered dose inhaler is used properly, however, only about 10% of the drug reaches the airways below the larynx. Nearly all the rest of the drug gets no further than the oropharynx and is swallowed. This swallowed portion may be absorbed from the gastrointestinal tract, but drugs such as inhaled corticosteroids are largely removed by first pass metabolism in the liver. Absorption directly from the lung bypasses liver metabolism.

The inhaler should be shaken and then fired into the mouth shortly after the start of a slow full inspiration. At full inflation the breath should be held for 10 seconds. The technique should be checked periodically. About a quarter of patients have difficulty using a metered dose inhaler and the problems increase with age. Arthritic patients can find it hard to activate the inhaler and may be helped by a Haleraid device, which responds to squeezing, or be given a breath actuated or dry powder system.

Breath actuated aerosol inhalers

Breath actuated metered dose inhalers are available for most classes of drug. The valve on the inhaler is actuated as the patient breathes in. The devices respond to a low inspiratory flow rate and are useful for those who have difficulty coordinating actuation and breathing. They require a propellant similar to that used in a standard inhaler.

CFC-free inhalers

Many current inhalers have moved from chlorofluorocarbon (CFC) propellants. The production, importation, and use of CFCs have been stopped in most developed countries because of the effect on the ozone layer. There is a temporary exemption for medical use under the Montreal Protocol, but CFC inhalers will be removed once adequate alternative products become available.

Alternative propellants

The challenge has been to develop safe alternatives that are as convenient, effective, and clinically equivalent. The process of development of alternative propellants has been more of a problem than first appreciated, particularly for inhaled steroids. Adaptations to the method of adding the drug to the propellant and to the valve and jet mechanisms have been necessary. Hydrofluoroalkanes 134 and 227 are used in the new devices.

This article is adapted from the 5th edition of the *ABC of Asthma in Adults*, which will be published later this year and available from www.hammicksbma.com

Inhalers deliver the drug direct to the airways

The mechanisms inside a metered dose inhaler

Elderly patients may find it difficult to use a metered dose inhaler

Short and long acting β agonists, inhaled steroids, and combinations are now available in inhalers with hydrofluoroalkanes. Each new device has to be tested carefully as total and regional delivery to the lung will differ with the new devices. The beclometasone product Qvar is prescribed at half the dose of a conventional metered dose inhaler because of its better lung deposition. Other preparations can be substituted at the same dose. Patients will notice differences in the speed of the aerosol cloud and taste.

The switch to CFC-free inhalers should be taken as an opportunity to review the patient's understanding and inhaler technique and general asthma management.

Spacer devices

The coordination of firing and inspiration becomes slightly less important when a short extension tube or spacer is used. This may help if problems are minor, and a larger reservoir removes the need for coordination of breathing and actuation. The inhaler is fixed into the chamber and the breath is taken through a one way valve at the other end of the chamber. Inhalation should be as soon as possible after each actuation, certainly within 30 seconds, and tidal breathing is as effective as deep breaths.

Pharyngeal deposition is greatly reduced as the faster particles strike the walls of the chamber, not the mouth. Evaporation of propellant from the larger, slower particles produces a small sized aerosol that penetrates further out into the lungs and deposits a greater proportion of drug beyond the larynx. This reduces the risk of oral candidiasis and dysphonia with inhaled corticosteroids and reduces potential problems with systemic absorption from the gastrointestinal tract. Spacers should be used routinely when doses of inhaled steroid above 800 μ g daily are given by metered dose inhaler.

The device is cumbersome, but this is no great disadvantage for twice daily treatment such as corticosteroids. Chambers have proved useful as a substitute for a nebuliser in acute asthma. Output characteristics of metered dose inhalers vary, and inhalers and extension tubes need to be matched appropriately. It cannot be assumed that results transfer to different combinations.

Electrostatic charge can reduce drug delivery. Chambers should be washed in detergent and left to air dry (rather than wiped dry) once a month and changed every 6-12 months. Metal chambers without static charge can also be used.

Dry powder inhalers

Dry powder inhalers of various types are available for β agonists, sodium cromoglicate, corticosteroids, anticholinergic drugs, and combinations. Because inspiratory airflow releases the fine powder many problems of coordination are avoided, and there are none of the environmental worries of metered dose inhalers.

The dry powder makes some patients cough, and the respiratory flow rate needed may be a problem with some devices. The problems of reloading for each dose have been eased by the development of multiple dose units with up to 200 doses, and many devices have a dose counter that helps the patient to know when the inhaler needs renewing and provides a compliance monitor.

Some dry powder devices such as the Turbohaler increase lung deposition and may allow a reduction in the prescribed dose.

An extension tube (spacer) used with a metered dose inhaler

Use of spacer devices

- Match the inhaler and spacer
- Inhale as soon as possible after each single actuation
- Empty the chamber by single large breaths or tidal breathing
- Clean chamber monthly
- Wash chamber in detergent and water and leave to dry
- Wipe any detergent from mouthpiece
- Replace spacer every 6-12 months

The Accuhaler has a convenient dose counter

Nebulisers

Nebulisers can be driven by compressed gas (jet nebuliser) or an ultrasonically vibrating crystal (ultrasonic nebuliser). They provide a way of giving inhaled drugs to those unable to use any other device—for example, very young children—or in acute attacks when inspiratory flow is limited.

Nebulisers also offer a convenient way of delivering a higher dose to the airways. Generally, about 12% of the drug leaving the chamber enters the lungs, but most of the dose stays in the apparatus or is wasted in expiration. Delivery depends on the type of nebuliser chamber, the flow rate at which it is driven, and the volume in the chamber. In most cases flow rates of less than 6 l/min in a jet nebuliser give too large a particle and nebulise too slowly. Some chambers have a reservoir and valve system to reduce loss to the surrounding room during expiration.

In many situations equivalent effects can be obtained with metered dose inhalers and a spacer but patients often have confidence in their nebuliser.

Tablets and syrups

Tablets and syrups are available for oral use. This route is necessary for theophyllines and leukotriene receptor antagonists, which cannot be inhaled effectively. Very young children who are unable to inhale drugs can take the sugar-free liquid preparations. Slow release tablets are used when prolonged action is needed, particularly for nocturnal asthma in which theophyllines have proved helpful. Various slow release mechanisms or long acting drugs have been developed to maintain even blood concentrations.

Tablets avoid the need to learn the coordination required for inhalers and might allow delivery to lung tissue beyond blocked airways but at the expense of potential side effects from body distribution.

Injections and infusions

Injections are used for the treatment of acute attacks.

Subcutaneous injections may be useful in emergencies when nebulisers are unavailable. Occasional patients with severe chronic asthma seem to benefit from the high levels of β stimulant obtained with subcutaneous infusion through a portable pump. Rates may need to be adjusted depending on severity. The infusion site is changed by the patient every one to three days.

The picture of the elderly woman using a metered dose inhaler is reproduced with permission of 3M.

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Competing interests: JR has received lecture fees from GSK and Astra-Zeneca.

BMJ 2005;331:504-6

The use of nebulisers must be associated with careful instructions on use and hygiene as well as arrangements for maintenance and support

Steady theophylline concentrations in the therapeutic range can be obtained with twice daily slow release preparations (D'Alonzo GE, et al, *Am Rev Respir Dis* 1990;142:84-90)

In severe cases β_2 agonists can be delivered by subcutaneous infusion